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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/161,680    09/28/98    BORNSCHEUER

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EXAMINER

KERR, K

ART UNIT

PAPER NUMBER

1652

DATE MAILED:

11/30/99

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
**09/161,680**

Applicant(s)  
**Bornscheuer et al.**

Examiner  
**Kathleen Kerr**

Group Art Unit  
**1652**

☒ Responsive to communication(s) filed on 11/18/98

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 1-9 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1-9 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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## DETAILED ACTION

### *Information Disclosure Statement*

1. The information disclosure statement filed 11/20/98 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. A copy of Harpes was not supplied and was, therefore, not considered. The reference to Winnacker was not a clear in its citation information and was, therefore, not considered. The consideration of all other documents is identified on applicant's copy of the Information Disclosure Citation (Form PTO-1449) included herein.

### *Objections to the Specification*

2. The disclosure is objected to because of the following informalities:
  - a. The title should be capitalized or bold font to indicate it more clearly.
  - b. On page 4, lines 25-26, "regio-, chemo-, or stereoselective or" should be deleted as a typographical error since it is repetitious.
  - c. On page 11, line 29, PFE is undefined although it is used throughout the text.

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- d. On page 13, line 4, applicant discloses "an overnight culture" with no more description implying a culture of *Escherichia coli* JM109 or DH5 $\alpha$  which harbors the plasmid 2792.1 described in the previous section. Applicant is requested to include this description of the culture on page 13, line 4 if this is the proper information. If applicant is referring to a different culture on page 13, line 4, applicant is requested to adjust the disclosure appropriately so that it is clear.
- e. On page 14, line 31, PFE-U1 is disclosed as a gene which is inconsistent with applicant's previous reference to PFE-U1 as a clone on page 14, line 10. Furthermore, on page 16, line 14, PFE-U3 is also referred to as a protein in addition to a clone and a gene. Applicant is requested to use appropriate biochemical language referring to the clone as PFE-U1 or -U3, the gene as the PFE gene from clone PFE-U1 or -U3, and the protein as a protein expressed by clone PFE-U1 or -U3.
- f. A brief description of the drawings is required in the text of the specification in a separately-labeled section.

### ***Objections to the Claims***

- 3. Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

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claim(s) in independent form. The limitation of prokaryotic and eukaryotic microorganisms encompasses all microorganisms and, as such, does not further limit Claim 1 from which it depends. Claim 3 is, therefore, will not be considered further in this examination.

***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 1, part c, the word "transmitting" is vague; in Claim 2, line 2, "returning the DNA" is also vague. The Examiner suggests alternate language, such as "extracting" and "transforming into" respectively, be used.
5. Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Both Claims 6 and 7 describe improper Markush groupings which contain elements that are not exclusive; for example, in Claim 6, a phosphatase is a member of the esterase family, and in Claim 7, a phytase is a member of the esterase family. The Examiner would like to recommend the Enzyme Commission numbers for assistance in classifying enzyme/substrate reactions ([http://www.genome.ad.jp/dbget-bin/get\\_htext?ECtable](http://www.genome.ad.jp/dbget-bin/get_htext?ECtable)).

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***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-2 and 4-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Greener et al. Greener et al. disclose the introduction of a cloned phosphatase gene into the *E. coli* strain XL1-Red (Stratagene, La Jolla, CA) for the purpose of introducing single, random point mutations into said gene, iterating the process for several generations to achieve the appropriate degree of mutation in said gene, and screening for phenotypic variants of said gene in a nonmutator host organism, specifically *E. coli*. The cloned gene specifically used in Greener et al. is alkaline phosphatase which is generally classified in the hydrolase family of enzymes (Enzyme Commission number EC 3.), further classified as an esterase, and as such specifically meets applicants' limitations in claims 5-7.

Although Greener et al. does not specifically define an increase in specific activity as a change in substrate specificity; it is inherently so in lieu of both applicants' specification and the generally accepted use of the term "substrate specificity" in the art. Greener et al. conclude that "these...mutations (as induced by the mutator strain method) result in a variant having higher specific activity..."; this conclusion is also held by the Examiner. On page 3, last paragraph, and continuing onto page 4 of the specification, applicants define an increase in activity (kcat) as a

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mode for achieving a higher substrate specificity (kcat/Km). In addition to this inherency in the term "substrate specificity," applicants' limitation in claim 8 to a selective enzymatic activity is also inherent in Greener et al. Simply by virtue of the fact that enzymes catalyze particular reactions, any enzyme-catalyzed reaction is selective to varying degrees. One might argue that enzymes, which can use a variety of substrates, are less selective, but no enzyme uses every substrate and therefore has some degree of selectivity. With this in mind, the limitation in applicants' claim 8 is easily qualified when the product of the method described is an active enzyme as found in Greener et al.

***Claim Rejections - 35 U.S.C. § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greener et al. (Methods in Molecular Biology 57:375) in view of Wilks et al. (Conference ref). Greener et al. disclose as described above in section 6. Greener et al. do not disclose their method resulting in a regio-, chemo-, or stereoselective enzymatic activity. Furthermore, Greener et al do not disclose using, nonmutator host microorganisms other than the Gram-negative bacteria, *E. coli*; however, the idea, set forth in the limitations of claim 4 of substituting Gram-positive bacteria, fungi, or

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yeast as microorganisms to express and screen the mutated gene instead of only *E. coli*, are well known in the art. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute Gram-positive bacteria, fungi, or yeast for *E. coli* as the microorganism for expression and/or screening because these substitute organisms are readily available, readily accept foreign DNA, and readily grow. Wilks et al. disclose the ability and motivation for one skilled in the art to rationally design and produce enzymes with new substrate specificities, particularly those specificities which enable enantiomeric enrichment of products for large-scale synthesis. Although Wilks et al. do not use applicants' random mutation method to produce these enzymes with new substrate specificities, the method by which mutation is achieved, whether rational or random, is irrelevant to the outcome of an enantiomerically selective enzymatic activity. Therefore, it would have been obvious to one skilled in the art at the time the invention was made to combine the teachings of Greener et al. and Wilks et al. to produce enzymes with regio-, chemo-, or stereoselective activities by methods of random mutagenesis and screening.

### ***Conclusion***

No claims are allowed in the instant application for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

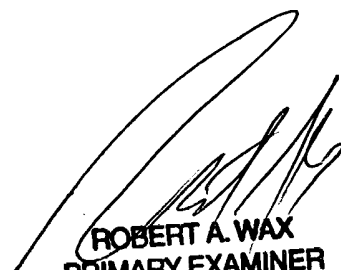


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Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Dr. Kathleen M. Kerr whose telephone number is (703) 305-1229. The Examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone number for this Group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



ROBERT A. WAX  
PRIMARY EXAMINER

KMK

November 22, 1999